

**PATENT** 

# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 05-363)

In the Application of:	)
Philip John Hogg	)
	) Examiner: TBD
Serial No.: 10/534,922	)
	) Group Art Unit: TBD
Filing Date: May 9, 2005	)
	) Confirmation No.: TBD
For: Induction of The Mitochondrial	)
Permeability Transition	)

#### TRANSMITTAL LETTER

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

In regard to the above identified application,

- 1. We are transmitting herewith the attached:
  - a) Information Disclosure Statement;
  - b) PTO Form 1449 and 99 references cited therein; and
  - c) return receipt postcard.
- 2. With respect to fees:
  - a) A fee is not required at this time.
  - b) Please charge any underpayment or credit any overpayment our Deposit Account, No. 13-2490.
- 3. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on August 8, 2005.

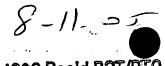
Respectfully submitted,

Date: August 8, 2005

Michael S. Greenfield Registration No. 37,142

McDonnell Boehnen Hulbert & Berghoff LLP 300 South Wacker Drive Chicago, IL 60606 (312)913-0001





# JC06 Rec'd PCT/PTO 11 AUG 2005

**PATENT** 

# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 05-363)

In the Application of:

Philip John Hogg

Serial No.: 10/534,922

Filing Date: May 9, 2005

For: Induction of The Mitochondrial

**Permeability Transition** 

Examiner: TBD

Group Art Unit: TBD

Confirmation No.: TBD

#### INFORMATION DISCLOSURE STATEMENT

Honorable Commissioner of Patents and Trademarks P.O. Box 1450 Alexandria, Virginia 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. Section 1.97 - 1.99, the Applicant wishes to make the following references of record in the above-identified application. This Information Disclosure Statement is in compliance with the continuing duty of candor as set forth in 37 C.F.R. Section 1.56. Copies of the cited references are enclosed. These references are also listed on the enclosed PTO Form 1449.

This statement is not a representation that the listed references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. Section 102 or Section 103.

Applicants do not believe any fee is due with this submission. If this belief be in error and the Patent Office determines that the fee prescribed in the relevant portion of 37 C.F.R. Section 1.97 is applicable, the undersigned attorney by his signature hereby authorizes any such fee to be debited from Deposit Account 13-2490.

#### **U. S. PATENTS**

1. Friedheim, et al., U.S. Patent No. 3,883,650, issued May 13, 1975.

#### **FOREIGN PATENT DOCUMENTS**

CERTIFICATE OF MAILING (37 C.F.R. 1.8a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the: Commissioner for Patents, P.O. Box 1450, Alexandria, NAC2313-1450, on August 8, 2005.

Date: August 8, 2005

lichael S. Greenfield

Copied from 10534992 on 11/07/2008

- 2. French Patent No. FR 2 781 674, published July 31, 1998.
- 3. PCT Patent No. WO 98/51297, published November 19, 1998.
- 4. PCT Patent No. WO 99/18798, published April 22, 1999.
- 5. PCT Patent No. WO 99/55344, published November 4, 1999.
- 6. PCT Patent No. WO 00/56742, published September 28, 2000.
- 7. PCT Patent No. WO 01/21628 A1, published March 29, 2001.

#### **OTHER DOCUMENTS**

- 8. Fairlamb, Alan H., et al., "Trypanothione is the Primary Target for Arsenical Drugs Against African Trypanosomes," *PNAS*, Vol. 86 (1989) pp. 2607-2611.
- 9. Fairlamb, Alan H. & Cerami, Anthony, "Metabolism and Functions of Trypanothione in the Kinetoplastida," *Annu. Rev. Microbiol.*, Vol. 46 (1992) pp. 695-729.
- 10. Cunningham, Mark L., et al., "Mechanism of inhibition of Trypanothione Reductase and Glutathione Reductase by Trivalent Organic Arsenicals," *FEBS*, Vol. 221 (1994) pp. 285-295.
- 11. Bhargava, Kuldeep K., et al., "Effect of Arsenical Drugs on Glutathione Metabolism of Litomosoides Carinii," Molecular and Biochemical Parasitology, Vol. 9 (1983) pp. 29-35.
- 12. Carter, Nicola S. & Fairlamb, Alan H., "Arsenical-Resistant Trypanosomes Lack an Unusual Adenosine Transporter," *Nature*, Vol. 361 (1993) pp. 173-176
- 13. Pisciotto, Patricia T. & Graziano, Joseph H., "Induction of Mucosal Glutathione Synthesis by Arsenic," *Biochemical et Biophysica Acta*, Vol. 628 (1980) pp. 241-243.
- 14. Lawrence, David A., et al., "Surface Thiols of Human Lymphocytes and Their Changes after In Vitro and In Vivo Activation," *Journal of Leukocyte Biology*, Vol. 60, (1996) pp. 611-618.
- 15. Ryser, Hugues J.-P., et al., "Cell Surface Sulfhydryls are Required for the Cytotoxicity of Diphtheria Toxin but not of Ricin in Chinese Hamster Ovary Cells," *Journal of Biological Chemistry*, Vol. 266, No. 28 (1991) pp. 18439-18442.
- 16. Mandel, Richard, et al., "Inhibition of a Reductive Function of the Plasma Membrane by Bacitracin and Antibodies Against Protein Disulfide-Isomerase," PNAS, Vol. 90 (1993) pp. 4112-4116.
- 17. Couët, Jacques, et al., "Cell Surface Protein Disulfide-Isomerase is Involved in the Shedding of Human Thyrotropin Receptor Ectodomain," *Biochemistry*, Vol. 35 (1996) pp. 14800-14805.
- 18. Krishna Rao, A. S. M. & Hausman, R. E., "cDNA for R-Cognin: Homology with a Multifunctional Protein," *PNAS*, Vol. 90 (1993) pp. 2950-2954.
- 19. Zai, Adrian, et al., "Cell-Surface Protein Disulfide Isomerase Catalyzes Transnitrosation and Regulates Intracellular Transfer of Nitric Oxide," *The Journal of Clinical Investigation*, Vol. 103, No. 3 (1999) pp. 393-399.
- 20. Essex, David W., et al., "Localization of Protein Disulfide Isomerase to the External Surface of the Platelet Plasma Membrane," *Blood*, Vol. 86, No. 6 (1995) pp. 2168-2173.
- 21. Essex, David W., et al., "Protein Disulphide Isomerase Mediates Platelet Aggregation and Secretion," *British Journal of Haematology*, Vol. 104 (1999) pp. 448-454.
- 22. Täger, Michael, et al., "Membrane-Bound Proteindisulfide Isomerase (PDI) is Involved in Regulation of Surface Expression of Thiols and Drug Sensitivity B-CLL Cells," *Experimental Hematology*, Vol. 25 (1997) pp. 601-607.

- Stathakis, Paul, et al., "Generation of Angiostatin by Reduction and Proteolysis of Plasmin: Catalysis by a Plasmin Reductase Secreted by Cultured Cells," J. Bio. Chem., Vol. 272, No. 33 (1997) pp. 20641-20645.
- 24. Stathakis, Paul, et al., "Angiostatin Formation Involves Disulfide Bond Reduction and Proteolysis in Kringle 5 of Plasmin," *J. Bio. Chem.*, Vol. 274, No. 13 (1999) pp. 8910-8916.
- 25. Bannai, Shiro & Tsukeda, Hohko, "The Export of Glutathione from Human Diploid Cells in Culture," J. Bio. Chem., Vol. 254, No. 9 (1979) pp. 3444-3450.
- 26. Holmgren, Arne, "Thioredoxin and Glutaredoxin Systems," J. Bio. Chem., Vol. 264, No. 24 (1989) pp. 13963-13966.
- 27. Rosén, Anders, et al., "A CD4<sup>+</sup> T Cell Line-Secreted Factor, Growth, Promoting for Normal and Leukemic B Cells, Identified as Thioredoxin," *International Immunology*, Vol. 7, No. 4 (1995) pp. 625-633.
- 28. Happersberger, Peter H., & Glocker, Michael O., "A Mass Spectrometric Approach to the Characterization of Protein Folding Reactions," Eur. Mass Spectrom, Vol. 4 (1998) pp. 209-214.
- 29. Halestrap, Andrew P., et al., "The Permeability Transition Pore Complex: Another View," *Biochimie*, Vol. 84 (2002) pp. 153-166.
- Desagher, Solange & Martinou, Jean-Claude, "Mitochondria as the Central Control Point of Apoptosis," Trends in Cell Biology, Vol. 10 (2000) pp. 369-377.
- 31. Fantin, Valeria R., et al., "A Novel Mitochondriotoxic Small Molecule that Selectively Inhibits Tumor Cell Growth," Cancer Cell, Vol. 2 (2002) pp. 29-42.
- 32. Belzacq, Anne-Sophie, et al., "The Adenine Nucleotide Translocator in Apoptosis," *Biochimie*, Vol. 84 (2002) pp. 167-176.
- 33. McStay, Gavin P., et al., "Role of Critical Thiol Groups on the Matrix Surface of the Adenine Nucleotide Translocase in the Mechanism of the Mitochondrial Permeability Transition Pore," *Biochem. J.*, Vol. 367 (2002) pp. 541-548.
- 34. Koch, Alisa Erika, "The Role of Angiogensis in Rheumatoid Arthritis: Recent Developments," *Ann. Rheum. Dis.*, Vol. 59 (2000) pp. 65-71.
- 35. Hayes, Andrew J., "Angioneogenesis in Rheumatoid Arthritis," The Lancet, Vol. 354 (1999) pp. 423-424.
- 36. Anonymous, "Arthritis: The Aging Populations of Developed Countries are Likely to present a Growing market for Arthritis Therapies," *Nature Biotechnology*, Vol. 18 (2000) pp. IT12-IT14.
- 37. Ades, Edwin W., et al., "HMEC-1: Establishment of an Immortalized Human Microvascular Endothelial Cell Line," The Journal of Investigative Dermatology, Vol. 99, No. 6 (1992) pp. 683-690
- 38. Andre, Harry A. M., et al., "Binding of Vascular Anticoagulant  $\alpha$  (VAC $\alpha$ ) to Planar Phospholipid Bilayers," *J. Bio. Chem.*, Vol. 265, No. 9 (1990) pp. 4923-4926.
- 39. Blankenberg, F.G. & Strauss, H. W., "Will Imaging of Apoptosis Play a Role in clinical Care? A tale of Mice and Men," *Apoptosis*, Vol. 6 (2001) pp. 117-123.
- 40. Dahmoun, M., et al., "Apoptosis, Proliferation, and Sex Hormone Receptors in Superficial Parts of Human Endometrium at the End of the Secretory Phase," *The Journal of Clinical Endocrinology & Metabolism*, Vol. 84, No. 5 (1999) pp. 1737-1743.
- 41. Daly, John M., et al., "Neu Differentiation Factor Induces ErbB2 Down-Regulation and Apoptosis of ErbB2-Overexpressing Breast Tumor Cells," *Cancer Research*, Vol. 57 (1997) pp. 3804-3811.

- 42. Donoghue, Neil, et al., "Presence of Closely Spaced Protein Thiols on the Surface of Mammalian Cells," *Protein Science*, Vol. 9, (2000) pp. 2436-2445.
- 43. Fisher, Karen L., et al., "Cloning and Expression of Human Tissue Factor cDNA," *Thrombosis Research*, Vol. 48 (1987) pp. 89-99.
- 44. Gottlieb, Roberta A. & Engler, Robert L., "Apoptosis in Myocardial Ischemia-Reperfusion," Ann. N. Y. Acad. Sci., Vol. 874 (1999) pp. 412-426.
- 45. Hofstra, Leo, et al., "Visualisation of Cell Death in vivo in Patients with Acute Myocardial Infarction," The Lancet, Vol. 356 (2000) pp. 209-212.
- 46. Huang, Xianming, et al., "Tumor Infraction in Mice by Antibody-Directed Targeting of Tissue Factor to Tumor Vasculature," *Science*, Vol. 275 (1997) pp. 547-550.
- 47. Jiang, Xing-Mai, et al., "Redox Control of Exofacial protein Thiols/Disulfides by protein Disulfide Isomerase," *J. Bio. Chem.*, Vol. 274, No. 4 (1999) pp. 2416-2423.
- 48. Ju, Shyr-Te, et al., "Molecular and Cellular Mech Regulating T and B Cell Apop Through Fax/FasL Interaction," *Intern, Rev. Immunol.*, Vol. 18 (1999) pp. 485-513.
- 49. Krams, Sheri M. & Martinez, Olivia M., "Apoptosis as a Mechanism of Tissue Injury in Liver Allograft Rejection," *Seminars in Liver Disease*, Vol. 18, No. 2 (1998) pp. 153-167.
- 50. Nihei, Oscar K., et al., "Pharmacologic Properties of P<sub>2Z</sub>/P2X<sub>7</sub> Receptor Characterized in Murine Dendritic Cells: Role on the Induction of Apoptosis," *Blood*, Vol. 96, No. 3 (2000) pp. 996-1004.
- 51. O'Reilly, Michael S., et al., "Angiostatin: A Novel Angiogensis Inhibitor That Mediates the Suppression of Metastases by a Lewis Lung Carcinoma," *Cell*, Vol. 79 (1994) pp. 315-328.
- 52. Parker, Jane E. & Mufti, Ghulam J., "The Role of Apoptosis in the Pathogenesis of the Myelodysplastic Syndromes," *Int. J. Hematol.*, Vol. 73 (2001) pp. 416-428.
- 53. Ramachandran, Anup et al., "Apoptosis in the Intestinal Epitheliam: Its Relevance in Normal and Pathophysiological Conditions," *Journal of Gastroenterology and Hepatology*, Vol. 15 (2000) pp. 109-120.

- 54. Riddles, Peter W., et al., "Reassessment of Ellman's Reagent," *Methods in Enzymology*, Vol. 91 (1983) pp. 50-61.
- 55. Rimon, Galia et al., "Rapid Communication: Increased Surface Phosphatidylserine Is an Early Marker of Neuronal Apoptosis," *Journal of Neuroscience Research*, Vol. 48 (1997) pp. 563-570.
- 56. Rupnow, B. A. & Know, S. J., "The Role of Radiation-Induced Apoptosis as a determinant of tumor Responses to radiation Therapy," *Apoptosis*, Vol. 4, No. 2 (1999) pp. 115-143.
- 57. Stefanec, Tihomir, "Endothelial Apoptosis, Could it Have a Role in the pathogenesis and Treatment of a Disease?," Chest, Vol. 117, No. 3 (2000) pp. 841-854.
- 58. Stone, Martin J., et al., "Recombinant Soluble Human Tissue Factor Secreted by Saccharomyces Cerevisiae and Refolded from Escherichia Coli Inclusion Bodies: Glycosylation of Mutants, Activty and Physical Characterization," Biochem J., Vol. 310 (1995) pp. 605-614.
- 59. Thompson, Craig B., "Apoptosis in the pathogenesis and Treatment of Disease," *Science*, Vol. 267 (1995) pp. 1456-1462.
- 60. Vermes, István, et al., "A Novel Assay for Apoptosis Flow Cytomertic Detection of Physphatidylserine Expression on Early Apoptoic Cells Using Fluorescein labeled Annexin V," *Journal of Immunological Methods*, Vol. 184 (1995) pp. 39-51.

- 61. Virginio, C., et al., "Kinetics of Cell Lysis, Dye Uptake and Permeability Changes in Cells Expressing the Rat P2X<sub>7</sub> Receptor," *Journal of Physiology*, Vol. 519 (1999) pp. 335-346.
- 62. Weissleder, Ralph, et al., "In Vivo Imaging of Tumors with Protease-Activated Near-Infrared Fluorescent Probes," *Nature Biotechnology*, Vol. 17 (1999) pp. 375-378.
- 63. Adams, Earle, et al., "Chemistry of Organometalloid Complexes with potential Antidotes: Structure of an Organoarsenic(III) Dithiolate Ring," *Inorg. Chem.*, Vol. 29 (1990) pp. 1500-1503.
- 64. Greenberg, N. M., et al., "Prostate Cancer in a Transgenic Mouse," PNAS, Vol. 92 (1995) pp. 3439-3443.
- 65. Hofstra, L., et al. "In Vivo Detection of Apoptosis in an Intracardiac Tumor," *JAMA*, Vol. 285, No. 14 (2001) pp. 1841-1842.
- 66. Kaufmann, Scott H., "Cell Death Induced by Topoisomerase-Targeted Drugs: More Questions Than Answers," *Biochimica et Biophysica Acta*, Vol. 1400 (1998) pp. 195-211.
- 67. Mattson, Mark P., "Apoptosis in Neurodegenerative Disorders," *National Review/Molecular Cell Biology*, Vol. 1 (2000) pp. 120-129.
- 68. Novia, Robert, "Protein Disulfide Isomerase: The Multifunctional Redox Chaperone of the Endoplasmic Reticulum," *Cell & Developmental Biology*, Vol. 10 (1999) pp. 481-493.
- 69. Pronk, Gijsbertus J., et al., "Requirement of an ICE-Like Protease for Induction of Apoptosis and Ceramide Generation by REAPER," *Science*, Vol. 271 (1996) pp. 80-810.
- 70. Thornberry, Nancy A. & Lasebnik, Yuri, "Caspases: Enemies Within," *Science*, Vol. 281 (1998) pp. 1312-1316.
- 71. Zhu, Huijun, et al., "An ICE-Like Protease is a Common Mediator of Apoptosis Induced by Diverse Stimuli in Human Monocytic THP.1 Cells," FEBS Letters, Vol. 374 (1995) pp. 303-308.
- 72. Bazarbachi, Ali, et al., "Aresenic Trioxide and Interferon-α Synergize to Induce Cell Cycle Arrest and Apoptosis in Human T-Cell Lymphotropic Virus Type I-Transformed Cells," *Blood*, Vol. 93, No. 1 (1999) pp. 278-283.
- 73. Gitler, Carlos, et al., "General Method to Identify and Enrich Vicinal Thiol Proteins Present in Intact Cells in the Oxidized, Disulfide State," *Analytical Biochemistry*, Vol. 252 (1997) pp. 48-55.
- 74. Beilstein Registry Number 21688.
- 75. Beilstein Registry Number 22377.
- 76. Beilstein Registry Number 51552.
- 77. Beilstein Registry Number 111664.
- 78. Beilstein Registry Number 116874.
- 79. Beilstein Registry Number 273946.
- 80. Beilstein Registry Number 358898.
- 81. Beilstein Registry Number 3126376.
- 82. Beilstein Registry Number 3129248.
- 83. Beilstein Registry Number 3135458.
- 84. Beilstein Registry Number 3139905.

- 85. Beilstein Registry Number 3141604.
- 86. Beilstein Registry Number 3152231.
- 87. Beilstein Registry Number 3233826.
- 88. Beilstein Registry Number 3235693.
- 89. Beilstein Registry Number 3254079.
- 90. Beilstein Registry Number 3273842.
- 91. Beilstein Registry Number 3275319.
- 92. Beilstein Registry Number 3285106.
- 93. Beilstein Registry Number 3293148.
- 94. Beilstein Registry Number 3296676.
- 95. Beilstein Registry Number 3298747.
- 96. Beilstein Registry Number 3319010.
- 97. Beilstein Registry Number 3341328.
- 98. Beilstein Registry Number 3344707.
- 99. Beilstein Registry Number 3531489.

Respectfully submitted,

McDonnell Boehnen Hulbert & Berghoff LLP

Date: August 8, 2005

Telephone:

Facsimile:

By:

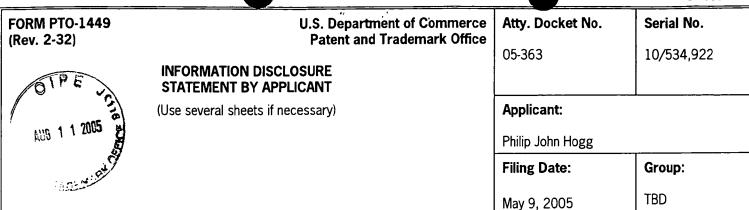
Michael S. Gree

Reg. No. 37.1/42

McDonnell Boehnen Hulbert & Berghoff LLP

300 South Wacker Drive

312-913-0001 312-913-0002 Chicago, IL 60606



#### **U.S. PATENT DOCUMENTS**

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	1.	3,883,650	05/13/75	Friedheim et al.			

#### **FOREIGN PATENT DOCUMENTS**

-		Document Number	Date	Country	Class	Sub Class	Translation Yes/No
	2.	FR 2 781 674	07/31/98	France			No
	3.	WO 98/51297	11/19/98	PCT			
	4.	WO 99/18798	04/22/99	PCT			
	5.	WO 99/55344	11/04/99	PCT			
	6.	WO 00/56742	09/28/00	PCT			
	7.	WO 01/21628 A1	03/29/01	PCT			

#### OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).

8.	Fairlamb, Alan H., et al., "Trypanothione is the Primary Target for Arsenical Drugs Against African Trypanosomes," PNAS, Vol. 86 (1989) pp. 2607-2611.
9.	Fairlamb, Alan H. & Cerami, Anthony, "Metabolism and Functions of Trypanothione in the Kinetoplastida," Annu. Rev. Microbiol., Vol. 46 (1992) pp. 695-729.
10.	Cunningham, Mark L., et al., "Mechanism of inhibition of Trypanothione Reductase and Glutathione Reductase by Trivalent Organic Arsenicals," FEBS, Vol. 221 (1994) pp. 285-295.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.





<u>~</u>	
11.	Bhargava, Kuldeep K., et al., "Effect of Arsenical Drugs on Glutathione Metabolism of Litomosoides Carinii," Molecular and Biochemical Parasitology, Vol. 9 (1983) pp. 29-35.
12.	Carter, Nicola S. & Fairlamb, Alan H., "Arsenical-Resistant Trypanosomes Lack an Unusual Adenosine Transporter," <i>Nature</i> , Vol. 361 (1993) pp. 173-176
13.	Pisciotto, Patricia T. & Graziano, Joseph H., "Induction of Mucosal Glutathione Synthesis by Arsenic," <i>Biochemical et Biophysica Acta</i> , Vol. 628 (1980) pp. 241-243.
14.	Lawrence, David A., et al., "Surface Thiols of Human Lymphocytes and Their Changes after In Vitro and In Vivo Activation," Journal of Leukocyte Biology, Vol. 60, (1996) pp. 611-618.
15.	Ryser, Hugues JP., et al., "Cell Surface Sulfhydryls are Required for the Cytotoxicity of Diphtheria Toxin but not of Ricin in Chinese Hamster Ovary Cells," <i>Journal of Biological Chemistry</i> , Vol. 266, No. 28 (1991) pp. 18439-18442.
16.	Mandel, Richard, et al., "Inhibition of a Reductive Function of the Plasma Membrane by Bacitracin and Antibodies Against Protein Disulfide-Isomerase," PNAS, Vol. 90 (1993) pp. 4112-4116.
17.	Couët, Jacques, et al., "Cell Surface Protein Disulfide-Isomerase is Involved in the Shedding of Human Thyrotropin Receptor Ectodomain," <i>Biochemistry</i> , Vol. 35 (1996) pp. 14800-14805.
18.	Krishna Rao, A. S. M. & Hausman, R. E., "cDNA for R-Cognin: Homology with a Multifunctional Protein," PNAS, Vol. 90 (1993) pp. 2950-2954.
19.	Zai, Adrian, et al., "Cell-Surface Protein Disulfide Isomerase Catalyzes Transnitrosation and Regulates Intracellular Transfer of Nitric Oxide," The Journal of Clinical Investigation, Vol. 103, No. 3 (1999) pp. 393-399.
20.	Essex, David W., et al., "Localization of Protein Disulfide Isomerase to the External Surface of the Platelet Plasma Membrane," <i>Blood</i> , Vol. 86, No. 6 (1995) pp. 2168-2173.
21.	Essex, David W., et al., "Protein Disulphide Isomerase Mediates Platelet Aggregation and Secretion," British Journal of Haematology, Vol. 104 (1999) pp. 448-454.
22.	Täger, Michael, et al., "Membrane-Bound Proteindisulfide Isomerase (PDI) is Involved in Regulation of Surface Expression of Thiols and Drug Sensitivity B-CLL Cells," Experimental Hematology, Vol. 25 (1997) pp. 601-607.
23.	Stathakis, Paul, et al., "Generation of Angiostatin by Reduction and Proteolysis of Plasmin: Catalysis by a Plasmin Reductase Secreted by Cultured Cells," <i>J. Bio. Chem.</i> , Vol. 272, No. 33 (1997) pp. 20641-20645.
24.	Stathakis, Paul, et al., "Angiostatin Formation Involves Disulfide Bond Reduction and Proteolysis in Kringle 5 of Plasmin," <i>J. Bio. Chem.</i> , Vol. 274, No. 13 (1999) pp. 8910-8916.
25.	Bannai, Shiro & Tsukeda, Hohko, "The Export of Glutathione from Human Diploid Cells in Culture," J. Bio. Chem., Vol. 254, No. 9 (1979) pp. 3444-3450.
26.	Holmgren, Arne, "Thioredoxin and Glutaredoxin Systems," J. Bio. Chem., Vol. 264, No. 24 (1989) pp. 13963-13966.
27.	Rosén, Anders, et al., "A CD4 <sup>+</sup> T Cell Line-Secreted Factor, Growth, Promoting for Normal and Leukemic B Cells, Identified as Thioredoxin," <i>International Immunology</i> , Vol. 7, No. 4 (1995) pp. 625-633.
28.	Happersberger, Peter H., & Glocker, Michael O., "A Mass Spectrometric Approach to the Characterization of Protein Folding Reactions," Eur. Mass Spectrom, Vol. 4 (1998) pp. 209-214.
29.	Halestrap, Andrew P., et al., "The Permeability Transition Pore Complex: Another View," Biochimie, Vol. 84 (2002) pp. 153-166.
	12. 13. 14. 15. 16. 17. 20. 21. 22. 23. 24. 25. 26. 27.

EXAMINER	DATE CONSIDERED
	,

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

McDonnell Boeinen Hulbert & Berghoff LLP 300 South Wacker Drive Chicago, Illinois 60606 Telephone (312) 913-0001 MBHB: 05-363 S/N: 10/534,922 Fung Date: May 9, 2005





	<u> </u>	
MADINA	30.	Desagher, Solange & Martinou, Jean-Claude, "Mitochondria as the Central Control Point of Apoptosis," <i>Trends in Cell Biology</i> , Vol. 10 (2000) pp. 369-377.
	31.	Fantin, Valeria R., et al., "A Novel Mitochondriotoxic Small Molecule that Selectively Inhibits Tumor Cell Growth," Cancer Cell, Vol. 2 (2002) pp. 29-42.
	32.	Belzacq, Anne-Sophie, et al., "The Adenine Nucleotide Translocator in Apoptosis," Biochimie, Vol. 84 (2002) pp. 167-176.
	33.	McStay, Gavin P., et al., "Role of Critical Thiol Groups on the Matrix Surface of the Adenine Nucleotide Translocase in the Mechanism of the Mitochondrial Permeability Transition Pore," <i>Biochem. J.</i> , Vol. 367 (2002) pp. 541-548.
	34.	Koch, Alisa Erika, "The Role of Angiogensis in Rheumatoid Arthritis: Recent Developments," Ann. Rheum. Dis., Vol. 59 (2000) pp. 65-71.
	35.	Hayes, Andrew J., "Angioneogenesis in Rheumatoid Arthritis," The Lancet, Vol. 354 (1999) pp. 423-424.
	36.	Anonymous, "Arthritis: The Aging Populations of Developed Countries are Likely to present a Growing market for Arthritis Therapies," Nature Biotechnology, Vol. 18 (2000) pp. IT12-IT14.
	37.	Ades, Edwin W., et al., "HMEC-1: Establishment of an Immortalized Human Microvascular Endothelial Cell Line," The Journal of Investigative Dermatology, Vol. 99, No. 6 (1992) pp. 683-690
	38.	Andre, Harry A. M., et al., "Binding of Vascular Anticoagulant $\alpha$ (VAC $\alpha$ ) to Planar Phospholipid Bilayers," <i>J. Bio. Chem.</i> , Vol. 265, No. 9 (1990) pp. 4923-4926.
	39.	Blankenberg, F.G. & Strauss, H. W., "Will Imaging of Apoptosis Play a Role in clinical Care? A tale of Mice and Men," Apoptosis, Vol. 6 (2001) pp. 117-123.
	40.	Dahmoun, M., et al., "Apoptosis, Proliferation, and Sex Hormone Receptors in Superficial Parts of Human Endometrium at the End of the Secretory Phase," The Journal of Clinical Endocrinology & Metabolism, Vol. 84, No. 5 (1999) pp. 1737-1743.
	41.	Daly, John M., et al., "Neu Differentiation Factor Induces ErbB2 Down-Regulation and Apoptosis of ErbB2-Overexpressing Breast Tumor Cells," Cancer Research, Vol. 57 (1997) pp. 3804-3811.
	42.	Donoghue, Neil, et al., "Presence of Closely Spaced Protein Thiols on the Surface of Mammalian Cells," <i>Protein Science</i> , Vol. 9, (2000) pp. 2436-2445.
	43.	Fisher, Karen L., et al., "Cloning and Expression of Human Tissue Factor cDNA," Thrombosis Research, Vol. 48 (1987) pp. 89-99.
	44.	Gottlieb, Roberta A. & Engler, Robert L., "Apoptosis in Myocardial Ischemia-Reperfusion," Ann. N. Y. Acad. Sci., Vol. 874 (1999) pp. 412-426.
	45.	Hofstra, Leo, et al., "Visualisation of Cell Death in vivo in Patients with Acute Myocardial Infarction," The Lancet, Vol. 356 (2000) pp. 209-212.
	46.	Huang, Xianming, et al., "Tumor Infraction in Mice by Antibody-Directed Targeting of Tissue Factor to Tumor Vasculature," Science, Vol. 275 (1997) pp. 547-550.
	47.	Jiang, Xing-Mai, et al., "Redox Control of Exofacial protein Thiols/Disulfides by protein Disulfide Isomerase," J. Bio. Chem., Vol. 274, No. 4 (1999) pp. 2416-2423.
	48.	Ju, Shyr-Te, et al., "Molecular and Cellular Mech Regulating T and B Cell Apop Through Fax/FasL Interaction," Intern, Rev. Immunol., Vol. 18 (1999) pp. 485-513.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

McDonnell Boeinen Hubert & Berghoff LLP 300 South Wacker Drive Chcago, Illinois 60606 Telephone (312) 913-0001





49.	Krams, Sheri M. & Martinez, Olivia M., "Apoptosis as a Mechanism of Tissue Injury in Liver Allograft Rejection," Seminars in Liver Disease, Vol. 18, No. 2 (1998) pp. 153-167.
50.	Nihei, Oscar K., et al., "Pharmacologic Properties of $P_{27}/P2X_7$ Receptor Characterized in Murine Dendritic Cells: Role on the Induction of Apoptosis," <i>Blood</i> , Vol. 96, No. 3 (2000) pp. 996-1004.
51.	O'Reilly, Michael S., et al., "Angiostatin: A Novel Angiogensis Inhibitor That Mediates the Suppression of Metastases by a Lewis Lung Carcinoma," Cell, Vol. 79 (1994) pp. 315-328.
52.	Parker, Jane E. & Mufti, Ghulam J., "The Role of Apoptosis in the Pathogenesis of the Myelodysplastic Syndromes," Int. J. Hematol., Vol. 73 (2001) pp. 416-428.
53.	Ramachandran, Anup et al., "Apoptosis in the Intestinal Epitheliam: Its Relevance in Normal and Pathophysiological Conditions," Journal of Gastroenterology and Hepatology, Vol. 15 (2000) pp. 109-120.
54.	Riddles, Peter W., et al., "Reassessment of Ellman's Reagent," Methods in Enzymology, Vol. 91 (1983) pp. 50-61.
55.	Rimon, Galia et al., "Rapid Communication: Increased Surface Phosphatidylserine Is an Early Marker of Neuronal Apoptosis," Journal of Neuroscience Research, Vol. 48 (1997) pp. 563-570.
56.	Rupnow, B. A. & Know, S. J., "The Role of Radiation-Induced Apoptosis as a determinant of tumor Responses to radiation Therapy," <i>Apoptosis</i> , Vol. 4, No. 2 (1999) pp. 115-143.
57.	Štefanec, Tihomir, "Endothelial Apoptosis, Could it Have a Role in the pathogenesis and Treatment of a Disease?," Chest, Vol. 117, No. 3 (2000) pp. 841-854.
58.	Stone, Martin J., et al., "Recombinant Soluble Human Tissue Factor Secreted by Saccharomyces Cerevisiae and Refolded from Escherichia Coli Inclusion Bodies: Glycosylation of Mutants, Activty and Physical Characterization," Biochem J., Vol. 310 (1995) pp. 605-614.
59.	Thompson, Craig B., "Apoptosis in the pathogenesis and Treatment of Disease," Science, Vol. 267 (1995) pp. 1456-1462.
60.	Vermes, István, et al., "A Novel Assay for Apoptosis Flow Cytomertic Detection of Physphatidylserine Expression on Early Apoptoic Cells Using Fluorescein labeled Annexin V," <i>Journal of Immunological Methods</i> , Vol. 184 (1995) pp. 39-51.
61.	Virginio, C., et al., "Kinetics of Cell Lysis, Dye Uptake and Permeability Changes in Cells Expressing the Rat $P2X_7$ Receptor," Journal of Physiology, Vol. 519 (1999) pp. 335-346.
62.	Weissleder, Ralph, et al., "In Vivo Imaging of Tumors with Protease-Activated Near-Infrared Fluorescent Probes," Nature Biotechnology, Vol. 17 (1999) pp. 375-378.
63.	Adams, Earle, et al., "Chemistry of Organometalloid Complexes with potential Antidotes: Structure of an Organoarsenic(III) Dithiolate Ring," <i>Inorg. Chem.</i> , Vol. 29 (1990) pp. 1500-1503.
64.	Greenberg, N. M., et al., "Prostate Cancer in a Transgenic Mouse," PNAS, Vol. 92 (1995) pp. 3439-3443.
65.	Hofstra, L., et al. "In Vivo Detection of Apoptosis in an Intracardiac Tumor," JAMA, Vol. 285, No. 14 (2001) pp. 1841-1842.
66.	Kaufmann, Scott H., "Cell Death Induced by Topoisomerase-Targeted Drugs: More Questions Than Answers," Biochimica et Biophysica Acta, Vol. 1400 (1998) pp. 195-211.
67.	Mattson, Mark P., "Apoptosis in Neurodegenerative Disorders," National Review/Molecular Cell Biology, Vol. 1 (2000) pp. 120-129.
68.	Novia, Robert, "Protein Disulfide Isomerase: The Multifunctional Redox Chaperone of the Endoplasmic Reticulum," Cell & Developmental Biology, Vol. 10 (1999) pp. 481-493.
	50. 51. 52. 53. 54. 55. 56. 57. 58. 60. 61. 62. 63. 64. 65. 66.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

McDonnell Boehnen Hulbert & Berghoff LLP 300 SOUTH WACKER DRIVE CHICAGO, BLUNOIS 60606 Copied from 10534992 on 11/07/2008 MBHB: 05-363

S/N: 10/534,922 Filing Date: May 9, 2005





& TRACE -		, , , , , , , , , , , , , , , , , , , ,
	69.	Pronk, Gijsbertus J., et al., "Requirement of an ICE-Like Protease for Induction of Apoptosis and Ceramide Generation by REAPER," Science, Vol. 271 (1996) pp. 80-810.
	70.	Thornberry, Nancy A. & Lasebnik, Yuri, "Caspases: Enemies Within," Science, Vol. 281 (1998) pp. 1312-1316.
	71.	Zhu, Huijun, et al., "An ICE-Like Protease is a Common Mediator of Apoptosis Induced by Diverse Stimuli in Human Monocytic THP.1 Cells," FEBS Letters, Vol. 374 (1995) pp. 303-308.
	72.	Bazarbachi, Ali, et al., "Aresenic Trioxide and Interferon-α Synergize to Induce Cell Cycle Arrest and Apoptosis in Human T-Cell Lymphotropic Virus Type I-Transformed Cells," <i>Blood</i> , Vol. 93, No. 1 (1999) pp. 278-283.
	73.	Gitler, Carlos, et al., "General Method to Identify and Enrich Vicinal Thiol Proteins Present in Intact Cells in the Oxidized, Disulfide State," Analytical Biochemistry, Vol. 252 (1997) pp. 48-55.
	74.	Beilstein Registry Number 21688.
	75.	Beilstein Registry Number 22377.
	76.	Beilstein Registry Number 51552.
	77.	Beilstein Registry Number 111664.
	78.	Beilstein Registry Number 116874.
	79.	Beilstein Registry Number 273946.
	80.	Beilstein Registry Number 358898.
	81.	Beilstein Registry Number 3126376.
•	82.	Beilstein Registry Number 3129248.
	83.	Beilstein Registry Number 3135458.
	84.	Beilstein Registry Number 3139905.
	85.	Beilstein Registry Number 3141604.
	86.	Beilstein Registry Number 3152231.
	87.	Beilstein Registry Number 3233826.
	88.	Beilstein Registry Number 3235693.
	89.	Beilstein Registry Number 3254079.
	90.	Beilstein Registry Number 3273842.
	91.	Beilstein Registry Number 3275319.
	92.	Beilstein Registry Number 3285106.
	93.	Beilstein Registry Number 3293148.
	94.	Beilstein Registry Number 3296676.
	95.	Beilstein Registry Number 3298747.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

McDonnell Boeinen Hulbert & Berghoff LLP 300 SOUTH WACKER DRIVE CHICAGO, LLINOIS 60606 TELEPHONE (312) 913-0001 Copied from 10534992 on 11/07/2008

MBHB: 05-363 S/N: 10/534,922 Filing Date: May 9, 2005





96.	Beilstein Registry Number 3319010.
97.	Beilstein Registry Number 3341328.
98.	Beilstein Registry Number 3344707.
99.	Beilstein Registry Number 3531489.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

١	McDonnell Boehnen Hulbert	& BERGHOFF LLP	
1	300 SOUTH WACKER DRIVE		
	CHICAGO, ILLINOIS 60606	71 * 10 10=01000 1110	
	TELEPHONE (312) 913-0001	Copied from 10534992 on 11/0	V / Z (R)X